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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/018,834	12/19/2001	Eric Edward Worrall	STHP002	4441

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EXAMINER	
LUCAS, ZACHARIAH	
ART UNIT	PAPER NUMBER
1648	5

DATE MAILED: 03/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/018,834	WORRALL, ERIC EDWARD	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 December 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,20 and 22* is/are rejected.

7)☒ Claim(s) *7-19,21 and 23-26* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claim Objections

1. Claims 7-19, 21, and 23-26 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim may not depend from another multiple dependant claim. See MPEP § 608.01(n).

As each of the identified claims is either a multiple dependant claim depending on another multiple dependant claim, or a claim depending on such a multiple dependant claim the claims have not been further treated on the merits.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims all read on methods of preserving a biologically-active material comprising mixing an aqueous suspension of the material with a chitosan solution, and adding the resulting solution to solution of trehalose. This new solution is then subjected to vacuum drying at less than atmospheric temperature and at "a temperature, initially no greater than 37° C, which is subsequently controlled not to fall to 0° C or below..." It is unclear what is meant by this last statement. The phrase could be read as indicating that the temperature of the solution at the initiation of the drying solution is less than or equal to 37° C, and is thereafter reduced, or

that the temperature is initially less than or equal to 37° C and thereafter may rise or fall provided that the temperature does not fall to, or below, 0° C. Clarification is required.

4. Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This claim reads on a method for the preservation of a biologically-active material wherein said material is Contagious Bovine Pleuropneumonia mycoplasma. The claim is rejected because Contagious Bovine Pleuropneumonia is the name of a disease caused by a mycoplasma bacterium, not the name of the bacterium itself (Mycoplasma mycoides). See e.g., Kiarie et al., Clin. Diag. Lab. Immunol. 3(6): 746-52. This rejection would be overcome if the bacteria name (Mycoplasma mycoides) were inserted in the place of the phrase Contagious Bovine Pleuropneumonia mycoplasma.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-3, 5, 6, 20, and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roser, U.S. Patent 5,149,653 (Roser I), in view of Illum et al. (U.S. Patent 6,391,318) and Chatfield (U.S. Patent 6,136,606), and in view of Roser et al., WO 96/40077 (Roser PCT), and Roser et al, U.S. Patent 6,221,575 (Roser II). Claims 1-6 have been described above. Claims 20

and 21 read on rehydratable compositions comprising trehalose is the form of a metastable glass matrix containing the dried biologically-active composition and chitosan.

Roser I teaches that the inclusion of trehalose in a viral medium during drying allows the virus to be preserved and reconstituted while retaining their immunogenic properties. Col 2, lines 1-8. Thus, the reference teaches that viral vaccines may be dried for later use when trehalose is incorporated into the viral solution during the drying phase. However, the reference teaches neither the inclusion of chitosan in the viral solution or the use of a vacuum drying method for the preservation of the viral vaccines.

Illum and Chatfield are both concerned with the efficacy of viral vaccines. More particularly, Illum teaches that Chitosan adjuvants are effective in increasing the immunogenicity of antigens in a vaccine. See e.g. Illum, column 2, lines 41-44, and claim 2. Chatfield also shows that chitosan can be an effective vaccine, including in composition comprising whole viruses. Chatfield, abstract, and claims 1 and 3. Thus, given the efficacy chitosan an a viral vaccine adjuvant, and the teachings of Roser I that immunogenic viral compositions may be preserved through drying in a trehalose composition, it would have been obvious to one of ordinary skill in the art to combine these teachings to use a trehalose composition in a process to preserve a composition comprising both an antigenic virus, and a chitosan adjuvant.

While Roser I teaches that trehalose allows viral compositions to be dried and preserved, it does not teach that they may be preserved through vacuum drying, or by vacuum drying such a composition at a temperature "initially no greater than 37° C." Such teachings are provided by Roser PCT and Roser II. Roser PCT teaches methods of vacuum drying and boiling biologically active compositions such that they may be preserved. Roser PCT, page 1,3, 12, and 14-18.

Among the compositions suggested by Roser PCT are viral and cellular compositions, including those comprising measles, mumps, polio, influenza, rubella, and yellow fever viruses. Pages 12-13. The reference also teaches on page 14 that immunogenic compositions preserved by the methods described therein preferable comprise an adjuvant.

With regard to the preservation method, Roser PCT teaches that by decreasing the pressure around the composition to be frozen, the boiling point of the composition is lowered, thereby preserving the integrity of the biologically-active substances. Pages 16-17. The drying step is performed until the residual moisture is between .1-5 percent. Page 18. The reference also teaches that residual moisture may be removed. (Thus, the reference teaches that the residual moisture may be less than 1%.) The reference teaches that such a process may be used to preserve the composition in a glass matrix composition. Such a composition may be reconstituted through rehydration (e.g. by adding a solvent to the matrix). Pages 18-19. However, unlike the claimed method, where the drying step is performed at 37° C or below, Rosen PCT states on page 17 that the preferable temperatures for performing the process are between 15 to 60, or 25-to 45 degrees Celsius.

Roser II is similarly concerned with the preservation of biological compositions. In this reference, a method is described for the vacuum drying of platelets such that they may be stored and preserved for a longer period of time. Column 1, line 54 to column 6, line 61.The reference teaches that "any method suitable for use in drying biological materials may be used" to dry the platelet composition. The reference teaches that the preferred method is vacuum drying, and that such a method may be conducted by decreasing the pressure to about 30 Torr (which is less than atmospheric pressure- 760 Torr). The reference further teaches that the temperature of the sample

is kept above 20 and below 38 degrees Celsius. In this, the reference teaches a range overlapping, and rendering obvious the claimed range of "no greater than 37 degrees." Thus, the above references cumulatively render the claimed method and compositions obvious.

It is noted that the references do not specifically teach the limitations of claims 5 and 6 of the claimed methods. However, given that the references teach the components used in the claimed processes, the ratios and acidity of the compositions are obvious as optimization of the claimed invention.

7. Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Roser I, in view of Illum, Chatfield, Roser PCT, and Roser II as applied to claims 1-3, 5, 6, 20, and 22 above, and further in view of Rweyemamu et al., Revue Scientifique et technologique 14(3), 593-601 (Medline abstract cited and provided) and Gombotz et al., U.S. Patent 5,900,238. This claim reads on the method of claim 1, wherein the biologically active material is Contagious Bovine Pleuropneumonia mycoplasma. For the purposes of this rejection, the claim is being read as though the identified bacteria were Mycoplasma mycoides, the mycoplasma that causes Contagious Bovine Pleuropneumonia. The teachings of the references other than Rweyemamu and Kiarie have been described above. These references teach the claimed method of vacuum drying a vaccine composition with the adjuvant chitosan in a trehalose containing solution.

The previously described references do not specifically teach that such the biologically-active material may be the described bacterium. They do teach, however, that bacteria may be so preserved. Roser PCT, page 12. Rweyemamu teaches a mycoplasma mycoides live bacteria vaccine that was preserved by freeze-drying. See, Medline abstract (teaching that the strain TI/44 is a known CBPP vaccine): and Kiarie et al., Clin. Diag. Lab. Immunol. 3(6): 746-52, at 746

(teaching that the TI bacterium is a strain of Mycoplasma mycoides used for CBPP vaccination). The Rweyemamu reference indicates that better methods of drying the vaccine are needed to minimize cell losses during the freeze drying process. Because the Roser references are concerned with the drying and preservation of biological material with a decreased loss of activity of the stored materials, it would have been obvious to those in the art to have combined the teachings of these references with the Rweyemamu reference to have improved the preservation method of this bacterium.

Further, chitosan is disclosed by the Illum reference as having an adjuvant effect, as well as acting as a carrier of vaccine antigens across mucosal membranes. Gombotz teaches that live or attenuated bacterial vaccines have been immunologically effective when mucosally administrated, but that effective delivery vehicles and soluble adjuvants are needed. As chitosan is disclosed in the art as being both a delivery vehicle across mucosal membranes, and an effective adjuvant, it would have been obvious to use chitosan in a live mycoplasma CBPP vaccine, and therefore to have incorporated the adjuvant into the preserved composition described above.

Conclusion

8. No claims are allowed.

9. The following prior art reference is made of record and is considered pertinent to applicant's disclosure. However, while relevant they are also not used as a basis for rejection for the stated reasons.

Bronshtein, WO 99/27071. This reference is substantially similar to the Roser PCT reference. It is concerned with the preservation of biologically active materials in a

matrix formed through vacuum drying. Pages 4-5. While it teaches the drying is carried out at sub-atmospheric pressures, it does not teach the temperature range used in the presently claimed method.

Clarke, WO 93/11220. This reference teaches that living bacteria may be preserved for later vaccine use by drying the cells in the presence of trehalose. Page 2.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 703-308-4240. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Z. Lucas
Patent Examiner
March 21, 2003

JAMES HOUSEL 3/23/03
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